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Intel Corporation c/o DARBY & DARBY P.C. P.O. BOX 770 CHURCH STREET STATION NEW YORK, NY 10008-0770			EXAMINER CROW, ROBERT THOMAS	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/750,315	<b>Applicant(s)</b> BERLIN ET AL.	
	<b>Examiner</b> Robert T. Crow	<b>Art Unit</b> 1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 September 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 18-23 and 36-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18-23 and 36-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 September 2007 has been entered.

### *Status of the Claims*

2. This action is in response to papers filed 18 September 2007 in which claims 18, 23, 36, 40, 41, 42, and 45-47 were amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 112, first paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 18-23 and 36-52 are under prosecution.

### *Claim Objections*

3. Claims 20, 38, 43, and 47 are objected to because of the following informalities: each of the claims recites the limitation "concentrations of nucleotides is" in lines 1-2 of each of the claims. This appears to be a typographical error. Appropriate correction is required.

*Claim Rejections - 35 USC § 112, First Paragraph*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 18-23 and 36-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This is a new matter rejection. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent claim 18, 36, 41, and 45 each recite "an unknown nucleic acid molecule" in line 2 of each of the claims.

Applicant has cited paragraph [0036], which reads "the sequence of the template strand 13 can be determined from the sequence of the nascent strand 16," for support of the amendment, stating that "persons skilled in the art would recognize that template strand 13 has a [sic] unknown nucleic acid molecule." However, the recitation does not necessarily mean that the template strand was unknown; i.e., an ordinarily skilled artisan can always deduce the sequence of the template strand from the nascent strand because the nascent strand is always complementary to the template strand from which it is synthesized. Thus, Applicant's citation of support does not necessarily require the template strand to be unknown. Furthermore, the phrase "comprising an unknown nucleic acid molecule" encompasses molecules wherein absolutely nothing is known about the sequence contained therein. In such a case, the ordinarily skilled artisan would not necessarily know a suitable primer for initiating synthesis of the nascent strand. Because Applicant's citation of paragraph [0036] requires a primer, at least some portion of the template is known. Thus, Applicant's citation does not support the embodiment of the claim wherein the template is completely unknown. In addition, a review of the specification yields no

recitation of an "unknown" nucleic acid molecule. Thus, the recitation of and "unknown" nucleic acid molecule constitutes new matter.

*Claim Rejections - 35 USC § 112, Second Paragraph*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 18-23 and 36-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-23 and 36-52 are indefinite in claims 18, 36, 41, and 45, each of which recites the limitation "the first and second channels" in line 6 of each of claims 18, 36, 41, and 45. The recitation "the first and second channels" lacks antecedent basis on the "inlet channel" and "outlet channel." It is suggested that the words "first" and "second" be changed to "inlet" and "outlet."

Claims 41-48 and 51-52 are indefinite in claims 41 and 45, each of which recites "the second Raman detection unit" in line 10 of each of claims 41 and 45. The recitation "the second Raman detection unit" lacks antecedent basis in the recitation of "a Raman detection unit" in each of claims 41 and 45. It is suggested that either the word "the" be changed to "a," or that the word "second" be deleted from the claims. For the purpose of examination, claims 41-48 and 51-52 are interpreted as requiring two Raman detectors; i.e., "a" Raman detection unit as well as "the second" Raman detection unit.

Claims 41-48 and 51-52 are further indefinite in the recitation "the Raman detection unit" in line 13 of each of claims 41 and 45 and in line 1 of each of claims 42 and 46. It is unclear if "the Raman detection unit" refers to the recitation of "a Raman detection unit" in line 8 of each of claims 41 and 45 or the recitation "the second Raman unit" in line 10 of each of claim 41 and 45.

Claim 43 is indefinite in the recitation "as they flow through the inlet channel" in line 2 of the claim. Because independent claim 41, upon which claim 43 depends, recites only one detection unit that is operably coupled only to the outlet channel (line 8 of claim 41), it is unclear how nucleotides are measured in the inlet channel when no Raman detector is required to be coupled to the inlet channel.

*Claim Rejections - 35 USC § 103*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 18-22, 36-39, and 41-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash (U.S. Patent Application Publication No. US 2002/0058273 A1, published 16 May 2002) in view of Davis (U.S. Patent Application Publication No US 2002/0102595 A1, published 1 August 2002) in view of Natan (U.S. Patent Application Publication No. US 2002/0142480 A1, published 3 October 2002).

Regarding claims 18 and 49, Shipwash teaches an apparatus. In a single exemplary embodiment, Shipwash teaches a reaction chamber containing a single template nucleic acid molecule attached to an immobilization surface; namely, a mixing channel, which is a reaction chamber, further comprising a bead having nucleic acids immobilized thereon (Figures 11 and 14, and paragraphs 0066 and 0255). The apparatus of Shipwash further comprises an inlet channel in fluid communication with the reaction chamber; namely, Figure 11, wherein the inlet channel comprises the channel having the digestion chamber (Figure 11), which is separate and distinct from the reaction chamber because the chamber is separate (paragraph 0043). Shipwash also teaches the apparatus comprises a separate and distinct outlet channel in fluid communication with the reaction chamber; namely, Figure 9, wherein the outlet channel is separate and downstream of the reaction chamber.

Shipwash also teaches a first Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman spectroscopy is used (paragraph 0174); thus, the first optical detector is a Raman detection unit. Shipwash also teaches a second Raman detection unit operably coupled to the outlet channel; namely, a second detector is coupled to the outlet of Figure 9. The second detector is a Raman spectrophotometer and Raman spectroscopy is used (paragraphs 0224 and 0174). The first and second detectors are therefore distinct and separate from the reaction chamber and are positioned before and after the reaction chamber.

Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0031) and uses Raman spectroscopy (paragraph 0174).

It is noted that the courts have held that "while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function." *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). In addition, "[A]pparatus claims cover what a device is, not what a device does." *Hewlett-*

*Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original). Therefore, the various uses recited in claim 18 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 18. Because the prior art teaches the structural elements of claim 18, the claim is obvious over the prior art.

While Shipwash also teaches detection of binding to an oligonucleotide aptamer (paragraph 0155), Shipwash does not teach an unknown nucleic acid or a polymerase and primer. Thus, Shipwash teaches a base apparatus that differs from the instantly claimed apparatus because Shipwash does not teach an unknown nucleic acid.

However, Davis teaches an apparatus comprising a reaction chamber containing a template comprising an unknown nucleic acid molecule attached to an immobilization surface; namely, an immobilized complex comprising a target nucleic acid, a primer nucleic acid, and a nucleic acid polymerase (i.e., claim 49; paragraph 0012). The immobilized complex is contained within a sample (i.e., reaction) chamber (paragraph 0057), and the target nucleic acid is subjected to sequencing so that the identity of the nucleic acid is determined (paragraph 0051); since the identity is to be determined, the nucleic acid molecule comprises an unknown nucleic acid molecule. Davis also teaches first and second illumination zones that are respectively upstream and downstream of the immobilized complex (paragraph 0006), wherein the first and second illumination zones each have a detection device operably coupled thereto (claim 15 of Davis). The detectors are configured to perform Raman spectroscopy because Raman scattering labels are detected (paragraph 0054). Davis also teaches the unknown nucleic acid has the added advantage of allowing genotyping of the unknown target nucleic acid (paragraph 0052), which aids in the detection of genetic diseases. Thus, Davis teaches the known technique of using immobilized unknown nucleic acids, polymerases, and primers in apparatuses having upstream and downstream Raman detectors.



It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising immobilized nucleic acids as taught by Shipwash with the immobilized unknown nucleic acids, polymerases, and primers of Davis with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of aiding in the detection of genetic diseases as a result of allowing genotyping of the unknown target nucleic acid as explicitly taught by Davis (paragraph 0054). In addition, it would have been obvious to the ordinary artisan that the known technique of using the unknown nucleic acids, polymerases, and primers of Davis could have been applied to the apparatus of Shipwash with predictable results because the unknown nucleic acids, polymerases, and primers of Davis predictably result in immobilized molecules suitable for analysis for genetic diseases.

Neither Shipwash nor Davis teach the Raman detection units configured for surface enhanced Raman spectroscopy. Thus, Shipwash in view of Davis teaches a base apparatus that differs from the instantly claimed apparatus because neither Shipwash nor Davis teaches detection units configured for surface enhanced Raman spectroscopy.

However, Natan teaches the Raman detection units configured for surface enhanced Raman spectroscopy (paragraph 0042) of nucleic acids (paragraph 0059) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules (i.e., nucleic acids) attached to the surface of a single metal nanoparticle in multiplexed assay formats (paragraph 0006), thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay. Thus, Natan teaches the known technique of using detection units configured for surface enhanced Raman spectroscopy.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units of

Shipwash in view of Davis with detectors of surface enhanced Raman spectroscopy as taught by Natan with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in an apparatus having the added advantage of allowing detection of nucleic acid molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats, thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as explicitly taught by Natan (paragraph 0006). In addition, it would have been obvious to the ordinary artisan that the known technique of using the detectors of surface enhanced Raman spectroscopy of Natan could have been applied to the apparatus of Shipwash in view of Davis with predictable results because the detectors of surface enhanced Raman spectroscopy of Natan predictably result in detectors usable for detecting biological molecules.

Regarding claim 19, the apparatus of claim 18 is discussed above. Shipwash also teaches each Raman detection unit is capable of detecting at least one nucleotide at the single molecule level; namely, single molecule detection is performed (paragraph 0168). Nucleotides are molecules; thus, because single molecule detection is performed, and because nucleotides are molecules, Shipwash teaches a unit capable of detecting a nucleotide at the single molecule level.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 19 (e.g., detecting nucleotides) fail to define additional structural elements to the device of claim 19. Because the prior art teaches the structural elements of claim 19, the claim is obvious over the prior art.

Regarding claim 20, the apparatus of claim 18 is discussed above. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0170) and uses Raman spectroscopy (paragraph 0174)..

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 20 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 20. Because the prior art teaches the structural elements of claim 20, the claim is obvious over the prior art.

Regarding claim 21, the apparatus of claim 18 is discussed above. Shipwash teaches nucleic acids are on metal particles in channels (paragraph 0043), which is interpreted as being in the inlet and outlet channels. Shipwash does not explicitly teach surface enhanced Raman spectroscopy active particles.

However, Natan teaches surface enhanced Raman spectroscopy active particles; namely, SERS active metal nanoparticles (paragraph 0017), which have the added advantages of being stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity (paragraphs 0007-0009). Thus, Natan teaches the known technique of using SERS nanoparticles.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units of Shipwash in view of Davis with the surface enhanced Raman spectroscopy active particles as taught by Natan with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in an apparatus having the added advantage of having particles that are stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity as explicitly taught by Natan (paragraph 0007-0009). In addition, it would have been obvious to the ordinary artisan that the known technique of using the SERS metal nanoparticles of Natan could have been applied to the apparatus of Shipwash in view of Davis with predictable results because the SERS metal nanoparticles of Natan predictably result in nanoparticles useful for detecting biological molecules.

Regarding claim 22, the apparatus of claim 18 is discussed above. Shipwash also teaches the inlet channel and outlet channel diameter is between about 100 and about 200 micrometers in diameter (paragraph 0210).

Regarding claims 36 and 50, Shipwash teaches an apparatus. In a single exemplary embodiment, Shipwash teaches a reaction chamber containing a single template nucleic acid molecule attached to an immobilization surface; namely, a mixing channel, which is a reaction chamber, further comprising a bead having nucleic acids immobilized thereon (Figures 11 and 14, and paragraphs 0066 and 0255). The apparatus of Shipwash further comprises an inlet channel in fluid communication with the reaction chamber; namely, Figure 11, wherein the inlet channel comprises the channel having the digestion chamber (Figure 11), which is separate and distinct from the reaction chamber because the chamber is separate (paragraph 0043). Shipwash also teaches the apparatus comprises a separate and distinct outlet channel in fluid communication with the reaction chamber; namely, Figure 9, wherein the outlet channel is separate and downstream of the reaction chamber.

Shipwash also teaches a first Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman spectroscopy is used (paragraph 0174); thus, the first optical detector is a Raman detection unit. Shipwash also teaches a second Raman detection unit operably coupled to the outlet channel; namely, a second detector is coupled to the outlet of Figure 9. The second detector is a Raman spectrophotometer and Raman spectroscopy is used (paragraphs 0224 and 0174). The first and second detectors are therefore distinct and separate from the reaction chamber and are positioned before and after the reaction chamber.

Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0031) and uses Raman spectroscopy (paragraph 0174).

As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 36 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 36. Because the prior art teaches the structural elements of claim 36, the claim is obvious over the prior art.

While Shipwash also teaches detection of binding to an oligonucleotide aptamer (paragraph 0155), Shipwash does not teach unknown nucleic acids, polymerases, and primers or particles (i.e., labels) in the separate inlet and outlet channels. Thus, Shipwash teaches a base apparatus that differs from the instantly claimed apparatus because Shipwash does not teach unknown nucleic acids, polymerases, and primers or labels (in the form of particles) in the separate inlet and outlet channels.

However, Davis teaches an apparatus comprising a reaction chamber containing a template comprising an unknown nucleic acid molecule attached to an immobilization surface; namely, an immobilized complex comprising a target nucleic acid, a primer nucleic acid, and a nucleic acid polymerase (i.e., claim 50; paragraph 0012). The immobilized complex is contained within a sample (i.e., reaction) chamber (paragraph 0057), and the target nucleic acid is subjected to sequencing so that the identity of the nucleic acid is determined (paragraph 0051); since the identity is to be determined, the nucleic acid molecule comprises an unknown nucleic acid molecule. Davis also teaches first and second illumination zones that are respectively upstream and downstream of the immobilized complex (paragraph 0006), wherein the first and second illumination zones each have a detection device operably coupled thereto (claim 15 of Davis). The detectors are configured to perform Raman spectroscopy because Raman scattering labels are detected (paragraph 0054). Davis further teaches dNTPs that are labeled and which are present in and detected in the first illumination zone and detected again in the second detection by the two Raman detectors (paragraph 0006). Davis also teaches the labels and unknown nucleic acids have the added advantage of allowing genotyping of the unknown target nucleic acid (paragraph 0052), which aids in the detection of genetic diseases. Thus, Davis teaches the known

technique of using immobilized unknown nucleic acids and labels in the inlet and outlet channels in apparatuses having upstream and downstream Raman detectors.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising immobilized nucleic acids as taught by Shipwash with the immobilized unknown nucleic acids, polymerases, and primers and labels in the inlet and outlet as taught by Davis with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of aiding in the detection of genetic diseases as a result of allowing genotyping of the unknown target nucleic acid as explicitly taught by Davis (paragraph 0054). In addition, it would have been obvious to the ordinary artisan that the known technique of using the unknown nucleic acids, polymerases, and primers and labels of Davis could have been applied to the apparatus of Shipwash with predictable results because the unknown nucleic acids, polymerases, and primers and labels of Davis predictably result in immobilized molecules suitable for analysis for genetic diseases.

Neither Shipwash nor Davis teach the Raman detection units configured for surface enhanced Raman spectroscopy, or that the labels are metal SERS labels. Thus, Shipwash in view of Davis teaches a base apparatus that differs from the instantly claimed apparatus because neither Shipwash nor Davis teaches detection units configured for surface enhanced Raman spectroscopy or SERS labels.

However, Natan teaches the Raman detection units configured for surface enhanced Raman spectroscopy (paragraph 0042) of nucleic acids (paragraph 0059) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules (i.e., nucleic acids) attached to the surface of the single metal nanoparticle in multiplexed assay formats (paragraph 0006), thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay. Natan also teaches surface enhanced Raman spectroscopy active particles; namely, SERS active metal

nanoparticles (paragraph 0017), which have the added advantages of being stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity (paragraphs 0007-0009). Thus, Natan teaches the known technique of using detection units configured for surface enhanced Raman spectroscopy and SERS labels.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units of Shipwash in view of Davis with detectors of surface enhanced Raman spectroscopy and SERS labels as taught by Natan with a reasonable expectation of success. The modification would result in the use of the SERS particles of Natan in place of the labels of Davis, which in turn results in SERS particles in both the inlet and outlet channels. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in an apparatus having the added advantage of allowing detection of nucleic acid molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats, thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as explicitly taught by Natan (paragraph 0006). The ordinary artisan also would have been motivated to make such a modification because said modification would have resulted in an apparatus having the additional added advantage of having particles that are stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity as explicitly taught by Natan (paragraph 0007-0009). In addition, it would have been obvious to the ordinary artisan that the known technique of using the detectors of surface enhanced Raman spectroscopy and SERS nanoparticles of Natan could have been applied to the apparatus of Shipwash in view of Davis with predictable results because the detectors of surface enhanced Raman spectroscopy and SERS nanoparticles of Natan predictably result in detectors and labels usable for detecting biological molecules.

Regarding claim 37, the apparatus of claim 36 is discussed above. Shipwash also teaches each Raman detection unit is capable of detecting at least one nucleotide at the single molecule level; namely,

single molecule detection is performed (paragraph 0168). Nucleotides are molecules; thus, because single molecule detection is performed, and because nucleotides are molecules, Shipwash teaches a unit capable of detecting a nucleotide at the single molecule level.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 37 (e.g., detecting nucleotides) fail to define additional structural elements to the device of claim 37. Because the prior art teaches the structural elements of claim 37, the claim is obvious over the prior art.

Regarding claim 38, the apparatus of claim 36 is discussed above. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0170) and uses Raman spectroscopy (paragraph 0174).

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 38 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 38. Because the prior art teaches the structural elements of claim 38, the claim is obvious over the prior art.

Regarding claim 39, the apparatus of claim 36 is discussed above. Shipwash also teaches the inlet channel and outlet channel diameter is between about 100 and about 200 micrometers in diameter (paragraph 0210).

Regarding claims 41 and 51, Shipwash teaches an apparatus. In a single exemplary embodiment, Shipwash teaches a reaction chamber containing a single template nucleic acid molecule attached to an immobilization surface; namely, a mixing channel, which is a reaction chamber, further comprising a bead having nucleic acids immobilized thereon (Figures 11 and 14, and paragraphs 0066 and 0255). The apparatus of Shipwash further comprises an inlet channel in fluid communication with the reaction chamber; namely, Figure 9, wherein the inlet channel comprises the channel having the digestion



chamber (Figure 9), which is separate and distinct from the reaction chamber because the chamber is separate (paragraph 0043). Shipwash also teaches the apparatus comprises a separate and distinct outlet channel in fluid communication with the reaction chamber; namely, Figure 9 show an outlet channel is separate and downstream of the reaction chamber.

Shipwash also teaches a Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman spectroscopy is used (paragraph 0174); thus, the first optical detector is a Raman detection unit. Shipwash also teaches a second Raman detection unit operably coupled to the outlet channel; namely, a second detector is coupled to the outlet of Figure 9. The second detector is a Raman spectrophotometer and Raman spectroscopy is used (paragraphs 0224 and 0174). The first and second detectors are therefore distinct and separate from the reaction chamber and are positioned before and after the reaction chamber. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the outlet channel; namely, the system detects concentration (paragraph 0031) and uses Raman spectroscopy (paragraph 0174).

As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 41 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 41. Because the prior art teaches the structural elements of claim 41, the claim is obvious over the prior art.

While Shipwash also teaches detection of binding to an oligonucleotide aptamer (paragraph 0155), Shipwash does not teach unknown nucleic acids, polymerases, and primers. Thus, Shipwash teaches a base apparatus that differs from the instantly claimed apparatus because Shipwash does not teach unknown nucleic acids, polymerases, and primers.

However, Davis teaches an apparatus comprising a reaction chamber containing a template comprising an unknown nucleic acid molecule attached to an immobilization surface; namely, an

immobilized complex comprising a target nucleic acid, a primer nucleic acid, and a nucleic acid polymerase (i.e., claim 51; paragraph 0012). The immobilized complex is contained within a sample (i.e., reaction) chamber (paragraph 0057), and the target nucleic acid is subjected to sequencing so that the identity of the nucleic acid is determined (paragraph 0051); since the identity is to be determined, the nucleic acid molecule comprises an unknown nucleic acid molecule. Davis also teaches a detection device operably coupled to a channel (Figure 1), wherein the detector is configured to perform Raman spectroscopy because Raman scattering labels are detected (paragraph 0054). Davis also teaches the unknown nucleic acid has the added advantage of allowing genotyping of the unknown target nucleic acid (paragraph 0052), which aids in the detection of genetic diseases. Thus, Davis teaches the known technique of using immobilized unknown nucleic acids, polymerases, and primers in apparatuses having a Raman detector.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising immobilized nucleic acids as taught by Shipwash with the immobilized unknown nucleic acids, polymerases, and primers of Davis with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of aiding in the detection of genetic diseases as a result of allowing genotyping of the unknown target nucleic acid as explicitly taught by Davis (paragraph 0054). In addition, it would have been obvious to the ordinary artisan that the known technique of using the unknown nucleic acids, polymerases, and primers of Davis could have been applied to the apparatus of Shipwash with predictable results because the unknown nucleic acids, polymerases, and primers of Davis predictably result in immobilized molecules suitable for analysis for genetic diseases.

Neither Shipwash nor Davis teach the Raman detection units configured for surface enhanced Raman spectroscopy. Thus, Shipwash in view of Davis teaches a base apparatus that differs from the

instantly claimed apparatus because neither Shipwash nor Davis teaches detection units configured for surface enhanced Raman spectroscopy.

However, Natan teaches the Raman detection units configured for surface enhanced Raman spectroscopy (paragraph 0042) of nucleic acids (paragraph 0059) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules (i.e., nucleic acids) attached to the surface of a single metal nanoparticle in multiplexed assay formats (paragraph 0006), thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay. Thus, Natan teaches the known technique of using detection units configured for surface enhanced Raman spectroscopy.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising Raman detection unit of Shipwash in view of Davis with detectors of surface enhanced Raman spectroscopy as taught by Natan with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in an apparatus having the added advantage of allowing detection of nucleic acid molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats, thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as explicitly taught by Natan (paragraph 0006). In addition, it would have been obvious to the ordinary artisan that the known technique of using the detectors of surface enhanced Raman spectroscopy of Natan could have been applied to the apparatus of Shipwash in view of Davis with predictable results because the detectors of surface enhanced Raman spectroscopy of Natan predictably result in detectors usable for detecting biological molecules.

Regarding claim 42, the apparatus of claim 41 is discussed above. Shipwash also teaches each Raman detection unit is capable of detecting at least one nucleotide at the single molecule level; namely,

single molecule detection is performed (paragraph 0168). Nucleotides are molecules; thus, because single molecule detection is performed, and because nucleotides are molecules, Shipwash teaches a unit capable of detecting a nucleotide at the single molecule level.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 42 (e.g., detecting nucleotides) fail to define additional structural elements to the device of claim 42. Because the prior art teaches the structural elements of claim 42, claim 42 is obvious over the prior art.

Regarding claim 43, the apparatus of claim 41 is discussed above. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the inlet channel and the outlet channel; namely, the system detects concentration (paragraph 0170) and uses Raman spectroscopy (paragraph 0174).

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 43 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 43. Because the prior art teaches the structural elements of claim 43, claim 43 is obvious over the prior art.

Regarding claim 44, the apparatus of claim 41 is discussed above. Shipwash also teaches the inlet channel and outlet channel diameter is between about 100 and about 200 micrometers in diameter (paragraph 0210).

Regarding claims 45 and 52, Shipwash teaches an apparatus. In a single exemplary embodiment, Shipwash teaches a reaction chamber containing a single template nucleic acid molecule attached to an immobilization surface; namely, a mixing channel, which is a reaction chamber, further comprising a bead having nucleic acids immobilized thereon (Figures 11 and 14, and paragraphs 0066 and 0255). The apparatus of Shipwash further comprises an inlet channel in fluid communication with the reaction chamber; namely, Figure 9, wherein the inlet channel comprises the channel having the digestion

chamber (Figure 9), which is separate and distinct from the reaction chamber because the chamber is separate (paragraph 0043). Shipwash also teaches the apparatus comprises a separate and distinct outlet channel in fluid communication with the reaction chamber; namely, Figure 9 show an outlet channel is separate and downstream of the reaction chamber.

Shipwash also teaches a Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman spectroscopy is used (paragraph 0174); thus, the first optical detector is a Raman detection unit.

Shipwash also teaches a second Raman detection unit operably coupled to the outlet channel; namely, a second detector is coupled to the outlet of Figure 9. The second detector is a Raman spectrophotometer and Raman spectroscopy is used (paragraphs 0224 and 0174). The first and second detectors are therefore distinct and separate from the reaction chamber and are positioned before and after the reaction chamber. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the outlet channel; namely, the system detects concentration (paragraph 0031) and uses Raman spectroscopy (paragraph 0174).

As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 45 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 45. Because the prior art teaches the structural elements of claim 45, the claim is obvious over the prior art.

While Shipwash also teaches detection of binding to an oligonucleotide aptamer (paragraph 0155), Shipwash does not teach unknown nucleic acids, polymerases, and primers or particles (i.e., labels) in the separate inlet and outlet channels. Thus, Shipwash teaches a base apparatus that differs from the instantly claimed apparatus because Shipwash does not teach unknown nucleic acids, polymerases, and primers or labels (in the form of particles) in the separate inlet and outlet channels.

However, Davis teaches an apparatus comprising a reaction chamber containing a template comprising an unknown nucleic acid molecule attached to an immobilization surface; namely, an immobilized complex comprising a target nucleic acid, a primer nucleic acid, and a nucleic acid polymerase (i.e., claim 52; paragraph 0012). The immobilized complex is contained within a sample (i.e., reaction) chamber (paragraph 0057), and the target nucleic acid is subjected to sequencing so that the identity of the nucleic acid is determined (paragraph 0051); since the identity is to be determined, the nucleic acid molecule comprises an unknown nucleic acid molecule. Davis also teaches an illumination zone that is downstream of the immobilized complex (paragraph 0006), wherein the illumination zone has a detection device operably coupled thereto (Figure 1). The detector is configured to perform Raman spectroscopy because Raman scattering labels are detected (paragraph 0054). Davis further teaches dNTPs that are labeled and which are present in and detected in the second detection by the Raman detector (paragraph 0006). Davis also teaches the labels and unknown nucleic acids have the added advantage of allowing genotyping of the unknown target nucleic acid (paragraph 0052), which aids in the detection of genetic diseases. Thus, Davis teaches the known technique of using immobilized unknown nucleic acids and labels in the inlet and outlet channels in apparatuses having upstream and downstream Raman detectors.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising immobilized nucleic acids as taught by Shipwash with the immobilized unknown nucleic acids, polymerases, and primers and labels in the outlet as taught by Davis with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of aiding in the detection of genetic diseases as a result of allowing genotyping of the unknown target nucleic acid as explicitly taught by Davis (paragraph 0054). In addition, it would have been obvious to the ordinary artisan that the known technique of using the unknown nucleic acids, polymerases, and primers of Davis could have been applied to the apparatus of

Shipwash with predictable results because the unknown nucleic acids, polymerases, and primers and labels of Davis predictably result in immobilized molecules suitable for analysis for genetic diseases.

Neither Shipwash nor Davis teach the Raman detection units configured for surface enhanced Raman spectroscopy, or that the labels are metal SERS labels. Thus, Shipwash in view of Davis teaches a base apparatus that differs from the instantly claimed apparatus because neither Shipwash nor Davis teaches detection units configured for surface enhanced Raman spectroscopy or SERS labels.

However, Natan teaches the Raman detection units configured for surface enhanced Raman spectroscopy (paragraph 0042) of nucleic acids (paragraph 0059) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules (i.e., nucleic acids) attached to the surface of the single metal nanoparticle in multiplexed assay formats (paragraph 0006), thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay. Natan also teaches surface enhanced Raman spectroscopy active particles; namely, SERS active metal nanoparticles (paragraph 0017), which have the added advantages of being stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity (paragraphs 0007-0009). Thus, Natan teaches the known technique of using detection units configured for surface enhanced Raman spectroscopy and SERS labels.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising two Raman detection units of Shipwash in view of Davis with detectors of surface enhanced Raman spectroscopy and SERS labels as taught by Natan with a reasonable expectation of success. The modification would result in the use of the SERS particles of Natan in place of the labels of Davis, which in turn results in SERS particles in both the inlet and outlet channels. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in an apparatus having the added advantage of allowing detection of nucleic acid molecules attached to the surface of a single metal nanoparticle in multiplexed

assay formats, thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as explicitly taught by Natan (paragraph 0006). The ordinary artisan also would have been motivated to make such a modification because said modification would have resulted in an apparatus having the additional added advantage of having particles that are stabilized against decomposition of the analyte in solvent and air, chemically inert, and easily centrifuged and redispersed without loss of SERS activity as explicitly taught by Natan (paragraph 0007-0009). In addition, it would have been obvious to the ordinary artisan that the known technique of using the detectors of surface enhanced Raman spectroscopy and SERS nanoparticles of Natan could have been applied to the apparatus of Shipwash in view of Davis with predictable results because the detectors of surface enhanced Raman spectroscopy and SERS nanoparticles of Natan predictably result in detectors and labels usable for detecting biological molecules.

Regarding claim 46, the apparatus of claim 45 is discussed above. Shipwash also teaches each Raman detection unit is capable of detecting at least one nucleotide at the single molecule level; namely, single molecule detection is performed (paragraph 0168). Nucleotides are molecules; thus, because single molecule detection is performed, and because nucleotides are molecules, Shipwash teaches a unit capable of detecting a nucleotide at the single molecule level.

In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 46 (e.g., detecting nucleotides) fail to define additional structural elements to the device of claim 46. Because the prior art teaches the structural elements of claim 46, claim 46 is obvious over the prior art.

Regarding claim 47, the apparatus of claim 45 is discussed above. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the outlet channel; namely, the system detects concentration (paragraph 0170) and uses Raman spectroscopy (paragraph 0174).



In addition, as noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 47 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 47. Because the prior art teaches the structural elements of claim 47, claim 47 is obvious over the prior art.

Regarding claim 48, the apparatus of claim 45 is discussed above. Shipwash also teaches the inlet channel and outlet channel diameter is between about 100 and about 200 micrometers in diameter (paragraph 0210).

11. Claims 23 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash (U.S. Patent Application Publication No. US 2002/0058273 A1, published 16 May 2002) in view of Davis (U.S. Patent Application Publication No. US 2002/0102595 A1, published 1 August 2002) in view of Natan (U.S. Patent Application Publication No. US 2002/0142480 A1, published 3 October 2002) as applied to claims 18 and 36 above, and further in view of Ogle (U.S. Patent No. 6,328,869 B1, issued 11 December 2001).

Regarding claims 23 and 40, the apparatus of claims 18 and 36 is discussed above in Section 10. While Shipwash also teaches the apparatus further comprises a mesh in the form of filters and grids that retain nanoparticles in the channels of the apparatus (paragraphs 0167 and 0270), and that metals are used to make the substrates for the apparatus (paragraph 0164), neither Shipwash, Davis, and Natan are silent with respect to the materials used for the mesh. Thus, Shipwash in view of Davis in view of Natan teaches a base apparatus that differs from the instantly claimed apparatus because Shipwash in view of Davis in view of Natan does not teach a metal mesh.

However, Ogle teaches an apparatus for macromolecule purification (Title) comprising a mesh comprising platinum; namely, a platinum-coated titanium expanded mesh, which has the added advantage of being self supported and inexpensive (column 8, lines 50-62). Thus, Ogle teaches the known technique of using a mesh comprising platinum.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising a mesh as taught by Shipwash in view of Davis in view of Natan with the platinum mesh of Ogle with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of being self supported and inexpensive as explicitly taught by Ogle (column 8, lines 50-62). In addition, it would have been obvious to the ordinary artisan that the known technique of using the platinum mesh of Ogle could have been applied to the apparatus comprising a mesh as taught by Shipwash in view of Davis in view of Natan with predictable results because the platinum mesh of Ogle predictably results in a mesh suitable for the filtration of biological macromolecules.

#### *Double Patenting*

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 18-19, 21, 36-37, 41-42, and 45-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-28 and 30 of copending Application No. 11/753,361 in view of Shipwash (U.S. Patent Application Publication No. US

2002/0058273 A1, published 16 May 2002) in view of Davis (U.S. Patent Application Publication No US 2002/0102595 A1, published 1 August 2002) and in view of Natan (U.S. Patent Application Publication No. US 2002/0142480 A1, published 3 October 2002). Both sets of claims are drawn to a reaction chamber, an inlet (i.e., a microfluidic channel) in fluid communication with the reaction chamber, an outlet channel (i.e., flow-through cell) in fluid communication with the channel (i.e., all three elements are fluidically connected via the reaction chamber), nanoparticles in the outlet (i.e., flow cell) and a Raman detection unit operably couple to the outlet (i.e., flow through chamber). The claims of the '361 Application do not require second Raman detection units, distinct channels, measurement of concentrations, or SERS particles.

However, Shipwash comprising an inlet channel in fluid communication with the reaction chamber; namely, Figure 9, wherein the inlet channel comprises the channel having the digestion chamber (Figure 9), which is separate and distinct from the reaction chamber because the chamber is separate (paragraph 0043). Shipwash also teaches the apparatus comprises a separate and distinct outlet channel in fluid communication with the reaction chamber; namely, Figure 9 show an outlet channel is separate and downstream of the reaction chamber.

Shipwash also teaches a Raman detection unit operably coupled to the inlet channel; namely, an optical detector is integrated onto the inlet digestion chamber (paragraph 0484), wherein Raman spectroscopy is used (paragraph 0174); thus, the first optical detector is a Raman detection unit. Shipwash also teaches a second Raman detection unit operably coupled to the outlet channel; namely, a second detector is coupled to the outlet of Figure 9. The second detector is a Raman spectrophotometer and Raman spectroscopy is used (paragraphs 0224 and 0174). The first and second detectors are therefore distinct and separate from the reaction chamber and are positioned before and after the reaction chamber. Shipwash also teaches the concentrations of nucleotides are measured by Raman spectroscopy as they flow through the outlet channel; namely, the system detects concentration (paragraph 0031) and uses Raman spectroscopy (paragraph 0174).

As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 41 (e.g., measuring concentration of nucleotides) fail to define additional structural elements to the device of claim 41. Because the prior art teaches the structural elements of the claim, the claim is obvious over the prior art. Shipwash also teaches the device has the added advantage of allowing parallel processing of many sample in an automated manner (Abstract).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus of the '361 claims with the structures taught by Shipwash to arrive at the instantly claimed invention with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of allowing parallel processing of many sample in an automated manner as explicitly taught by Shipwash (Abstract).

Davis teaches an apparatus comprising a reaction chamber containing a template comprising an unknown nucleic acid molecule attached to an immobilization surface; namely, an immobilized complex comprising a target nucleic acid, a primer nucleic acid, and a nucleic acid polymerase (i.e., claim 51; paragraph 0012). The immobilized complex is contained within a sample (i.e., reaction) chamber (paragraph 0057), and the target nucleic acid is subjected to sequencing so that the identity of the nucleic acid is determined (paragraph 0051); since the identity is to be determined, the nucleic acid molecule comprises an unknown nucleic acid molecule. Davis also teaches a detection device operably coupled to a channel (Figure 1), wherein the detector is configured to perform Raman spectroscopy because Raman scattering labels are detected (paragraph 0054). Davis also teaches the unknown nucleic acid has the added advantage of allowing genotyping of the unknown target nucleic acid (paragraph 0052), which aids in the detection of genetic diseases.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising immobilized nucleic acids of the

'361 Application in view of Shipwash with the immobilized unknown nucleic acids, polymerases, and primers of Davis to arrive at the instantly claimed apparatus with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in an apparatus having the added advantage of aiding in the detection of genetic diseases as a result of allowing genotyping of the unknown target nucleic acid as explicitly taught by Davis (paragraph 0054).

Natan teaches the Raman detection units configured for surface enhanced Raman spectroscopy (paragraph 0042) of nucleic acids (paragraph 0059) with the added advantage that surface enhanced Raman spectroscopy allows detection of molecules (i.e., nucleic acids) attached to the surface of a single metal nanoparticle in multiplexed assay formats (paragraph 0006), thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the apparatus comprising Raman detection unit of the '361 Application in view of Shipwash in view of Davis with detectors of surface enhanced Raman spectroscopy as taught by Natan to arrive at the instantly claimed apparatus with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in an apparatus having the added advantage of allowing detection of nucleic acid molecules attached to the surface of a single metal nanoparticle in multiplexed assay formats, thereby increasing the sensitivity of the detection and increasing the number of different molecules detectable in a single assay, as explicitly taught by Natan (paragraph 0006).

This is a provisional obviousness-type double patenting rejection.

*Response to Arguments*

14. Applicant's arguments filed 18 September 2007 (i.e., the "Remarks") have been fully considered but are moot in view of the new ground(s) of rejection necessitated by the amendments.

*Conclusion*

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jehanne Sitton/  
Primary Examiner  
11/29/2007

Robert T. Crow  
Examiner  
Art Unit 1634

